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Chapter

Cervical Cancer Elimination by 2030: The "SMASH" Strategy of Raj © A Global Public Health Treatise

Rajamanickam Rajkumar

Abstract

Cervical cancer is a leading cancer among women, being the second most gynecological cancers in the developing countries, accounting for about 6 million new cases every year and 3.5 million deaths. The Cervical cancer is easily detectable by simple screening tests, like visual inspection methods, pap smear examination, and the recent HPV DNA test methods. If the precancer conditions are diagnosed, treatment can be done by ablation or excisional methods. The women can be followed by periodic cervical biopsy examinations, ideally once in 6 months for 3 years. If, at the end of 3 years, there is no evidence of cervical precancer, then the women will not develop invasive cancer stages. The HPV vaccination of adult and adolescent girls, offer more than 90% protection against Cervical Cancer. Thus, Cervical cancers are early detectable, effectively treatable and successfully preventable. The author, having been the Principal Investigator for one of the largest Cervical Cancer Screening programs in India, at Ambillikai, Tamil Nadu, India, during 2000–2007, which was in collaboration with the International Agency for Research on Cancer – IARC / WHO. The program was successful in reducing the Incidence Rate of Cervical Cancer by 25% and Mortality Rate due to Cervical Cancer, by 35% in a span of 5 years. From the experiences of this "Proof of Concept" project, the author has advocated, "SMASH" strategy of Raj©, for Cervical Cancer Elimination by 2030, which is deliberated in detail, in this chapter. Hope that, this will serve as a Global Public Health Treatise, for the health care planners and providers in particular and the community at large, worldwide.

Keywords: Cervical precancer, HPV vaccination, screening methods, Precancer treatment, Elimination strategy

1. Introduction

Cervical cancer is the fourth leading cause of cancer in women throughout the world. It is estimated that 604 000 new cases occur, every year, in the world (WHO 2020). About, 342 000 women die of Cervical cancer, per year. To stop this malady and suffering in women, and to prevent the tragic deaths, the WHO declared a strategy for Cervical Cancer Elimination CCE by 2030. There are three main targets, which will achieve that Goal.

- 1. To Vaccinate 90% of eligible girls against HPV
- 2. To Screen 70% of eligible women at least twice in their lifetime
- 3. To effectively treat 90% of those with a positive screening test for Cervical precancer lesions and also treatment & palliative care for invasive cancers

This chapter analysis the strategies that could be followed to achieve these targets. It is a proof of concept, "SMASH" strategy of Raj, for Cervical Cancer Elimination ©

S = Screening

M = Menstrual Health

A = Awareness

S = Sexual health

H = HPV Vaccination

The chapter explains the implementation of the above strategy, especially in low and middle income countries with limited, constrained resource settings.

Hence, this chapter and the contents of the book, serve as a "Global Public Health Treatise".

The Cervical cancer is preventable, detectable at very early stages and can be effectively treated at Precancer and Cancer stages.

Cervical Cancer is the only Cancer in the History of Mankind, to have been targeted for Elimination, at Global level.

The WHO, during May, 2018, called all the Nations, to take up the the challenge of Elimination of Cervical Cancer.

On 17th November, 2020, the WHO launched officially, the Global strategy to Accelerate the Elimination of Cervical Cancer, as a public health problem, by 2030 [1].

2. Screening

Screening is method in which, simple tests are applied to an apparently healthy women, to diagnose early changes in the Uterine cervix, the Precancer lesions, also called Dysplasias or Cervical Intraepithelial Neoplasis-CIN.

The Precancer lesions are caused by the persistent infections by Human Papilloma Virus HPV, the oncogenic strains, especially 16 and 18.

The main screening modalities are:

- 1. HPV DNA tests
- 2. Pap smear examinations
- 3. Visual Inspection methods by using Acetic acid-VIA, and or Lugol's iodine -VILI

There are two methods, globally followed, in screening and treatment

- 1. Screen and Treat approach ST
- 2. Screen, Triage and Treat approach **STT**

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2.1 ST

Screen and treat - ST approach, involves the treatment of the Precancer lesions on the basis of the positive First Primary Test.

2.2 STT

Screen, Triage and Treat - STT approach, involves the treatment on the basis ofof a Positive Primary Test, supported by the Second Test, which also becomes positive, followed by Colposcopy / Biopsy, and, after confirmation of the diagnosis, treatment is offered.

2.3 ST

In the screening and treatment ST, approach, the women undergoes treatment in a single visit, during which, the primary test is performed and treatment is offered for the positive result. The treatment of pre cancer lesions can be done by Cryotherapy, Cold coagulation, Large Loop Excision of Transformation Zone - LLETZ or Large Loop Electro Excision Procedure - LEEP, Cold Knife Conisation - CKC and Laser Ablation.

2.4 STT

In the the Screen Triage and Treat - STT approach, if the primary test is positive, then the woman is subjected for Colposcopy examination and guided Biopsy. Depending on the Second test and Biopsy results, the woman is treated for the Cervical Pre cancer lesions.

If the Primary test is positive and the second Triage test is negative, then the women needs to be meticulously followed up.

2.5 Recommendations

The recommendation by WHO is the use of HPV DNA test as the Primary test. This is applicable for both 'See and Treat ST' and 'See, Triage and Treat STT' approaches.

In the See and Treat approach, a positive HPV DNA test would lead to Treatment.

In the See, Triage and Treatment approach, the positive HPV DNA test is followed by Triage tests like HPV Genotyping, VIA – VILI, Colposcopy, and Cytoloigy. If a Triage test is also Positive, then we proceed on to treatment.

For HPV Testing the cervical cells can be collected by the Health care workers, in clinical / community settings, with all medical facilities and precautions.

The other way is to educate women and train them in Self collecting techniques, which are acceptable, affordable and available methods.

The ideal age for screening is 30–49 years. After 50 years, if two consecutive tests are negative, screening may be stopped, but the local health policy guidelines have to be followed.

If the HPV DNA testing is used as the Primary screening method, the regular Screening interval can be 5–10 years.

For other Primary tests like Pap smear, VIA-VILI, the regular screening interval is 3 years.

Screening of eligible women, even once or twice in their life time, if effective in preventing Cervical Cancer.

Women diagnosed with CIN lesions should be treated within 6 months of diagnosis. The recommended methods of treatment are excisional, in the form of LEEP (Large loop Electro Excision Procedure) or LLETZ (Large Loop Excision of Transformation Zone). The other method of treatment is Cold Knife Conisation - CKC, and this method is preferred when the margins are reported an questionable in the Histo Pathology reports.

If there is a delay of more than 6 months, the woman has to be reassessed and treated appropriately.

Future Developments in Screening Tests.

2.6 Molecular level

Nucleic Acid Amplification Tests (NAAT):

- 1. High risk HPV DNA NAAT
- 2. mRNA
- 3. DNA Methylation
- 4. Protein Biomarkers HPV Antibodies, Oncoproteins

2.7 Cytology level

- 1. Conventional Pap Smear
- 2. Liquid-based Cytology LBC
- 3. Dual staining to identify p16 and Ki-67

2.8 Visual inspection level

- 1. Visual Inspection VIA, VILI Naked Eye, Magnifying lens, Colposcopy, Camera
- 2. Automated Visual Evaluation of Digital Images Artificial Intelligence

The recommendations of Screening Protocols have been advocated by WHO, after analysis with priority questions using PICO format (P- Population, I-Intervention, C-Comparator, O-Outcome).

The Goal of Elimination of Cervical Cancer, by 2030, fixes a target of 70% of all the eligible women, to undergo Screening, which can be achieved by using the above Procedures and Protocols [2].

3. Menstrual health

3.1 Menstrual health day: MHD, 28th may

Menstrual Health Day - MHD, was celebrated all over the World, on 28th May, 2021. This is a Global movement to create awareness on Good Menstrual Practices. This was first initiated by WASH UNITED, an NGO in Germany, during year 2014.

Every year, this MHD is celebrated with a dedicated theme. The Theme for 2021, is, "Action and Investment in Menstrual Hygiene and Health."

Removing the social taboo, creating awareness on menstrual hygiene, are the main objectives.

3.2 National period day: NPD, 10th October

The National Period Day - NPD, is another movement for Menstrual Health activities, throughout the world. This is celebrated on 10th of October, every year. The activities include provision of menstrual hygiene products and sanitary facilities. The lack of these comes under the topic for work focus, Menstrual Poverty or Period Poverty.

3.3 The national tampon day- NPT, 12th May

A women spends about 7–8 years in Menstruation and related problems, in her life time, and yet more than 70% of women, especially living in developing countries, face Period Poverty. It is estimated that more than 800 million women and girls menstruate every day. They still face the problems of taboo, social discrimination, lack of knowledge, non availability and non affordability of sanitary pads, soap and water facilities, privacy in working and educational places, and Gender Equity issues, which need to be addressed by the Government and Non Government Organizations [3, 4].

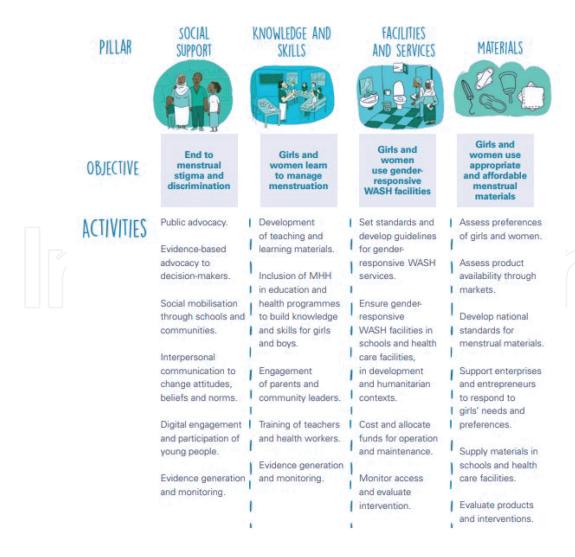


Figure 1.
UNICEF frame work for menstrual health services [5].

3.4 UNICEF: role in menstrual health

The UNICEF focuses upon the issues like Gender inequality-discrimination, Socio Cultural and Economic barriers, and to meet the unmet needs in Menstrual Health.

Menstrual poverty has many consequences like restriction of mobility and freedom in the work place and educational establishments, thus affecting their literacy life and work productivity, causing psychological problems like stress, anxiety and related disorders. To solve the problems of Menstrual Health, the UNICEF focuses on the following 4 strategic areas:

- 1. Gather Social support
- 2. Educational programs for developing Knowledge and Skills
- 3. Mobilize resources and develop programs
- 4. Provide materials and sanitary napkins and meet the Unmet needs of women during menstruation

The UNICEF primarily work through Governments and Voluntary Organizations in various countries for the improvement of Menstrual Health (**Figure 1**) [6, 7].

4. Awareness

Facts about Cervical cancer [8].

- 1. Cervical cancer is the cancer occurring at the mouth of the womb, the Uterus. The squmo epithelial cells undergo cancerous changes in the form of Dysplasias of various grades, in the transformation zone, which is called Precanncer lesions and later it undergoes uncontrolled multiplication called Hyperplasia, which becomes Invasive Cancer.
- 2. The women at risk are those who develop persistent infection by Human Papiloma Virus HPV 16 and 18
- 3. The Risk factors for developing HPV infections are poor menstrual hygiene, poor sexual hygiene, early onset of sexual activity, many sexual partners, unsafe abortions, use of Oral Contraceptive Pills- OCPs, Smoking
- 4. Cervical cancer screening is an effective method for the diagnosis of Precancer stages. If efficient treatment is offered for the Precancer lkesions, the disease gets cured and the women never develop invasive cancer
- 5. Screening methods are HPV DNA testing, Pap smear, Visual Inspection methods VIA / VILI
- 6. Confirmation of the diagnosis is made by Colposcopoy and directed biopsies
- 7. Diagnosis of Precancer conditions are made, which are called Dysplasias or Cervical Intraepithelial Neolpasias CIN

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- 8. The treatment modalities for Precancer lesions are Cryotherapy, Cold coagulation, Loop Electro Excision Procedure LEEP or Large Loop Excision of Transformation Zone LLETZ, Cold Knife Conization CKC, Laser Ablation
- 9. HPV Vaccination, for adult and adolescent girls is a sure method of Cervical cancer prevention
- 10. National and International efforts are made to Eliminate Cervical Cancer by the year 2030.

5. Sexual health

5.1 Important medical advice for good sexual health

- 1. Hygiene is keeping the body parts clean and cared so that physically healthy interactions can be made with the sex partner [9]
- 2. Good and clean habits are conducive for social health
- 3. Clean and well groomed body, helps in the prevention, cure of infections.
- 4. Good body boosts and maintain positive mental, psychological health
- 5. Good hygiene and cleanliness of sexual parts are important for safe and healthy sex, like cleaning the sexual organs with soap and water, before and after sexual activity.
- 6. Use of Condoms is very important and effective to prevent HPV Transmission. Also, it prevents the transmission of infections like HIV, Hepatitis, Gonorrhea, Candidiasis, Trichomonas and other sexually transmitted infections.

5.2 Oral sex

This sexual practice involves the oral stimulation of the sexual parts. Many people prefer this type of sex, because it avoids pregnancy. But due to the uncleanliness and bad hygiene of the sexual parts, many diseases are transmitted, including HIV, HPV, and other sexually transmitted fungal and bacterial diseases.

Therefore, cleaning the sexual parts before and after oral sex activity is very important to prevent disease transmission.

5.3 Menstrual hygiene

During menstrual periods, the uterus undergoes physiological changes which predisposes the cervis to invasion of organisms and infections. Therefore, its essential to maintain good hygiene and healthy practices during periods.

6. Human papilloma virus - HPV

Human Papilloma Virus infections are one of the most common infections in women in the reproductive age group. The prevalence of HPV infections is estimated to be 11.7% (Age adjusted) worldwide. There are more than 200 strains of

Туре	Age of administration	Dose	Schedule*	Route	Site	Cold chain	Availability
Gardasil (quadrivalent vaccine)	Girls and women: 9 through 26 years; males: 9 through 26 years	0.5 ml of liquid suspension	0, 2 and 6 months	Intramuscular injection	Deltoid region of upper arm or high anterolateral aspect of thigh	2-8°C (shelf life: 36 months)	Single dose vial (0.5 ml) in a package of 1, 10 and 100 vials
Cervarix (bivalent vaccine)	Girls and women: 9 through 26 years	0.5 ml of liquid suspension	0, 1 and 6 months	Intramuscular injection		2-8°C (shelf life: 36 and 48 months)	Single and two dose (0.5 ml and 1.0 ml vial); package of 1, 10 and 100 vials
Gardasil 9 (9vHPV)	Girls and women: 9 through 26 years; males: 9 through 26 years	0.5 ml of liquid suspension	0, 2 and 6 months	Intramuscular injection	Deltoid region of upper arm or high anterolateral aspect of thigh	2-8°C	Single dose vial (0.5 ml) 1 and 10 vials

*Girls<15 years (9-13 years) require two doses at least 6 months apart but within 12-15 months of first dose; girls>15 years or immune-compromised (e.g., HIV) women require three doses for full protection. HPV: Human papillomavirus

Figure 2.HPV vaccine schedule and other details: [10].

HPV, but the Oncogenic strains are HPV 16 and 18. More than 80% of the women have the risk of getting HPV infections in their life time. But most of the infections undergo spontaneous regression. In 1980, Zur Hausen, described the causal relationship of HPV infections and development of Cervical cancer. HPV infections cause other cancers of Oropharynxl, Anus, Vagina, Vulva and Penis.

6.1 Prevention and control strategies

- 1. HPV Vaccination
- 2. Screening
- 3. Treatment of Precancer lesions
- 4. Follow up for 3 years with 6 monthly Cervical biopsies
- 5. Declare cure at the end of 3 years if the Histo Pathology reports of the cervical biopsies indicate 'No Evidence of Disease'.

6.2 HPV vaccines

- 1. Quadrivalent vaccine: HPV types 6,11,16 and 18
- 2. Nine valent vaccine: HPV types 6,11,16,18,31,33,45,52,58

Protection rate = 70–90%.

The Nine valent vaccine offers protection against Cervical cancer and also, Anal, Vaginal, Vulval, Penile and Oropharyngeal cancers (**Figure 2**).

7. Conclusion

As conclusion, the author chooses to high light the newly developed, motivational slogan "ILLUMINATE – PARTICIPATE- ELIMINATE".

We have to *ILLUMINATE* our knowledge and skills about the facts of Cervical cancer, especially understand that *Primordial prevention*, can be achieved by preventing HPV in the community through HPV Vaccination. *Primary prevention* can be achieved by Health Promotion and Specific protection, by maintaining good Menstrual and Sexual Health. *Secondary prevention* can be achieved by "Early

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diagnosis and Treatment", by screening and treatment of Precancer stages and cure of the lesions, thus preventing them from developing in to invasive cancer stages.

Tertiary prevention is by Palliative care and disability limitation and rehabilitation.

The next step is to **PARTICIPATE** in awareness and health education programs, HPV Vaccination camps, Screening and treatment programs, ensuring and encouraging compliance by the community for the medical guidance and follow up schedules.

To **ELIMINATE**, is to reduce the prevelance of Cervical cancer to less than 4/100,000, by self motivation, community commitment and Global policy and political will.

To conclude, we will Illuminate, all our buildings by **TEAL LIGHT on**November 17th, every year, to symbolize ourselves as Community Captains, for Elimination of Cervical Cancer, all over the world, by 2030.



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